

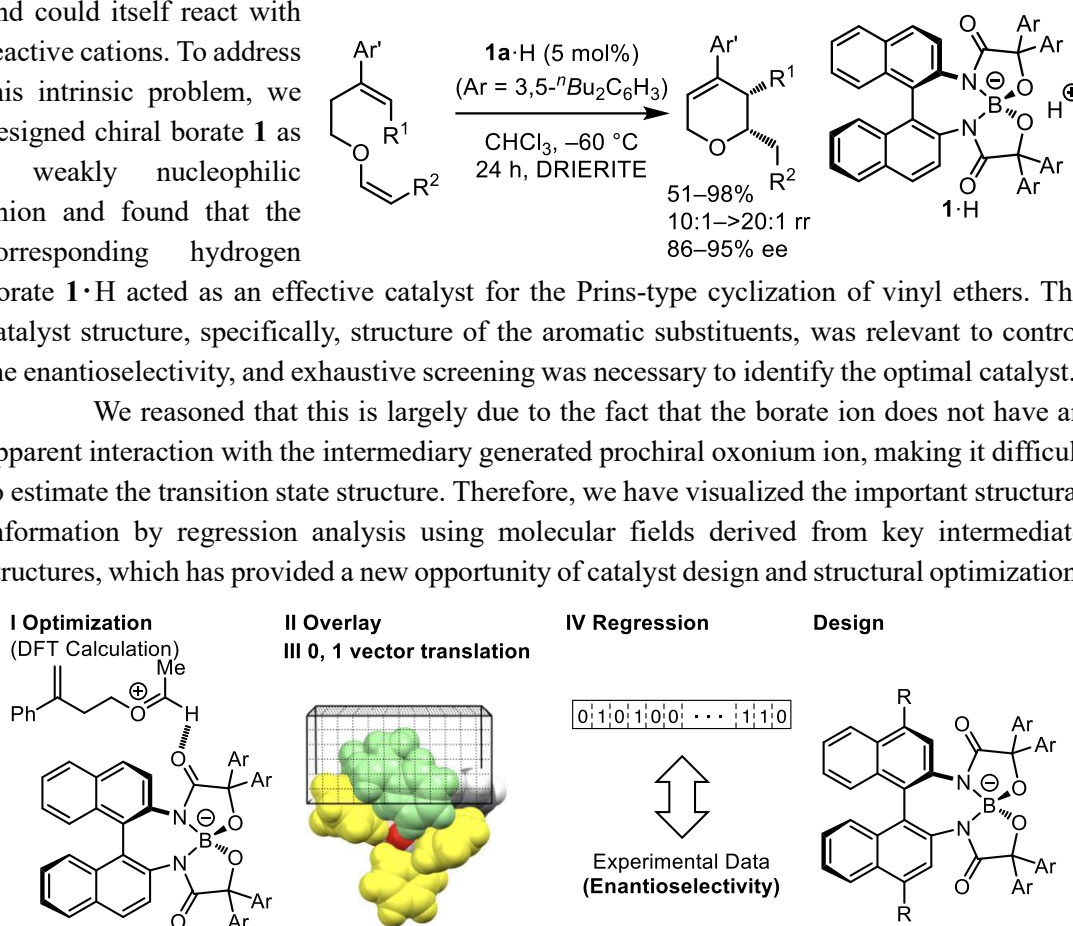
## Elucidation of the Stereocontrol Mechanism in Chiral Borate Catalysis toward Data-Driven Catalyst Design

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Prochiral cations are fundamental reactive species in organic synthesis and, upon reacting with nucleophiles, their enantiotopic faces should be precisely discriminated for obtaining stereochemically defined products. While ion-pairing with a chiral anion represents a direct and powerful approach for implementing this general mode of absolute stereocontrol, it is still underdeveloped because most of the existing chiral anions have innate nucleophilicity and could itself react with reactive cations. To address this intrinsic problem, we designed chiral borate **1** as a weakly nucleophilic anion and found that the corresponding hydrogen borate **1·H** acted as an effective catalyst for the Prins-type cyclization of vinyl ethers. The catalyst structure, specifically, structure of the aromatic substituents, was relevant to control the enantioselectivity, and exhaustive screening was necessary to identify the optimal catalyst.<sup>1</sup>

We reasoned that this is largely due to the fact that the borate ion does not have an apparent interaction with the intermediary generated prochiral oxonium ion, making it difficult to estimate the transition state structure. Therefore, we have visualized the important structural information by regression analysis using molecular fields derived from key intermediate structures, which has provided a new opportunity of catalyst design and structural optimization.



1) Uruguchi, D.; Ueoka, F.; Tanaka, N.; Kizu, T.; Takahashi, W.; Ooi, T. *Angew. Chem. Int. Ed.* **2020**, *59*, 11456.